

103(a) in view of Ganderton et al. in view of EP 0 786 526 (Kato et al.) are respectfully traversed.

The technical problem underlying the present invention can be formulated as to provide a process for preparing a carrier consisting of individual, not agglomerated, particles having a median diameter  $> 90 \mu\text{m}$  and a perfectly smooth surface, e.g. with a surface rugosity  $\leq 1.1$  upon determination of its fractal dimension (*see*, page 10, lines 25-27, and page 11, lines 9-10, of the present specification). The problem is solved by providing a process comprising the step of subjecting the particles to repeated stages of wetting with a solvent and drying in a high-speed mixer granulator characterized in that the wetting is carried out with a short-chain aliphatic alcohol or a water-alcohol mixture as the solvent.

Such an apparatus is designed and normally used for agglomerating solid particles and not for smoothing them individually (*see*, page 11, lines 15-18, of the present specification).

The present inventors have found that under certain conditions of use, it is possible to alter the surface characteristics of the carrier particles for inhalation use, without causing their agglomeration into granules or pellets (*see*, page 12, lines 3-14, of the present specification).

Moreover, as a result of the presently claimed process the fine particles present in the powder prior to smoothing are eliminated from the end product (*see*, page 13, lines 3-7, of the present specification). The presence of such fine particles can be detrimental to the flowability of the powder (*see*, page 9, lines 27-28, of the present specification).

Kato et al. discloses spherical particles made substantially of lactose having high surface smoothness with low abrasiveness, which are in the form of granules (*see*, page, line 56). Said granules ***are obtained by granulating powdered lactose*** (*see*, page, line 57).

For the production of the lactose spherical particles of Kato et al. (granules), the sprayed solution (in the centrifugal tumbling apparatus) may be water alone or if desired, a small amount of a water-soluble polymer may be dissolved therein, or an aqueous lactose

solution may be added. However, water alone is usually preferred (see, page 6, lines 23-30). Kato et al. is completely silent about the use of a solvent which is either an alcohol or a water-alcohol mixture.

In Kato et al. it is also disclosed that spherical particles have ideal characteristics as nuclei for controlled-release drugs, since they do not have the problem of complete resistance to disintegration as do spherical particles composed mainly of crystalline cellulose, but instead have suitable disintegration properties. Kato et al. also discloses that, since the lactose spherical particles have excellent surface smoothness and abrasion resistance as a result of fixation treatment of their surface, greater *granulating* and coating efficiency is possible for production of sustained-release preparations (see, page 10, lines 3-20).

Therefore Kato et al. teaches the preparation of particles in the form of *granules*, *i.e.* particles which are obtained from *agglomeration by granulation* of smaller particles, said granules being suitable for controlling the release of drugs and improving the resistance to disintegration of sustained-release formulations.

As recognized in the Office Action, Ganderton et al. lacks the teaching of a method of producing smooth carrier particles utilizing a high-speed granulator using an alcohol or a water-alcohol mixture as a solvent. Since the aim of the present invention is to make *individual (not agglomerated)* particles with a smooth surface as a carrier for inhalation of micronized drugs and not to make *granules* suitable for controlling the release of drugs and improving the resistance to disintegration of sustained-release formulations, it is respectfully submitted that the teachings of Kato et al. are not relevant to the presently claimed process, and hence the skilled person would not combine the teachings of Ganderton et al. and Kato et al.

Even if, by following the reasoning in the Office Action, one of skill in the art would have been motivated to combine the teachings of Ganderton et al. and Kato et al., he would not have reached the solution of the present invention without undue burden, *i.e.*

- the use of an apparatus which is designed and normally used for agglomerating solid particles (a high-speed granulator),
- the use of particular conditions (wetting the particles with an alcohol or a water-alcohol mixture as a solvent),

for preparing individual, not agglomerated, smooth particles to be used as a carrier for inhalation of micronized drugs.

For all of these reasons, the rejections are improper and should be withdrawn.

The rejection of Claims 22-29 and 32-33 under the judicially-created doctrine of obviousness-type double patenting in view of Claims 1-12 of U.S. Patent No. 6,780,508 (“the ‘508 patent”) has been obviated by appropriate amendment. As the Examiner will note, Claim 22 has been amended to incorporate the limitations of canceled Claim 30. Applicants respectfully submit that the present claims are patentable over the ‘508 patent for the same reasons Claim 30 was not rejected.

The rejection of Claims 26 and 27 under 35 U.S.C. § 112, second paragraph, has been obviated by appropriate amendment. As the Examiner will note, these claims have been amended such that they are free of the criticisms outlined on page 3 of the Office Action.

Applicants acknowledge the Examiner’s comments in regard to trademarks on page 2 of the Office Action. In this regard, it is submitted that the phrase “rotating-chamber mixer” given on page 22, lines 10-11, of the present specification is a sufficient generic description of the trademark TURBULA®. Similarly, it is submitted that the phrase “powder inhaler” given on page 22, line 25 of the present specification is a sufficient generic description for the trademark PULVINAL®.

U.S. Application No. 10/806,240  
Reply to Office Action dated October 16, 2006

Applicants submit that the application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.



---

Stephen G. Baxter  
Attorney of Record  
Registration No. 32,884

Customer Number  
**22850**

Tel: (703) 413-3000  
Fax: (703) 413-2220